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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,583	11/16/2001	Syed Z. Salahuddin	30418.2US01	3552

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EXAMINER	
FORD, ALLISON M	
ART UNIT	**PAPER NUMBER**
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/991,583	SALAHUDDIN, SYED Z.	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *13-27 and 29-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-12 and 28) in the reply filed on 12 March 2007 is acknowledged. The traversal is on the ground(s) that search and examination of all three inventive groups would not place an undue burden on the examiner. This is not found persuasive because as shown in the restriction requirement, the three different inventive groups are directed each to distinct subject matter; a reference which would anticipate or render obvious claims of one group would not necessarily anticipate or render obvious claims of another group. The different inventions each had different classifications, which is demonstrative of the divergent searches which would need to be conducted for each invention. Additionally a thorough search of all non-patent literature related to each of the distinct groups would, in fact, pose a serious burden on the examiner. The requirement is still deemed proper and is therefore made FINAL.

Claims 1-38 remain pending in the instant application, of which claims 13-27 and 29-38 are withdrawn from consideration as being directed to non-elected subject matter; claims 1-12 and 28 have been considered on the merits.

Priority

Acknowledgement is made of applicant's claim for priority to provisional application 60/249,762, filed 17 November 2000.

Information Disclosure Statement

The information disclosure statement filed 2 May 2002 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature

publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. Reference "A2" Arima et al, "Effects of Extracellular Matrix on Rat Kupffer Cell Functions in Vitro," *Cells of the hepatic Sinusoid*, 7:68-69 (1999), was not found in the application file, nor was it found upon a search by the Examiner. The remaining references on the IDS have been considered and initialed. If Applicants desire for *Arima et al* to be considered and listed on the face of any resulting patent, it is required that a copy be provided in response to this Office Action, as well as a subsequent IDS citing the reference for initialing by the Examiner.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Applicants' claims are directed to a composition comprising a culture of replicating macrophages, wherein at least some of the macrophages have undergone cell division during culture *in vitro*. Dependent claims further limit the time period during which the cells must have undergone division. Other dependent claims further define the macrophages as being phagocytic, staining positive for non-specific esterase and acid-phosphatase, expressing CD68, not expressing TGF-beta, being human macrophages, being non-transformed, being from a source other than a tumor, or being from a non-embryonic animal. Other dependent claims require the macrophages to be Kupffer cells.

It is noted that the instant claims are directed to a product: a composition comprising replicating macrophages. However, claims 1-12 include a 'wherein clause' which states that at least some of the macrophages must have previously undergone cell division during culture *in vitro*. Such 'wherein' (or 'whereby') clauses are only to be given weight when they state a condition that is material to

patentability, such as imparting structural or other physical properties to the claimed product. In the instant case, requiring the cells in the composition to *have previously* undergone cell division is not interpreted as imparting any unique physiological properties to the macrophages present in the claimed composition, a review of the specification also fails to point out or describe any properties or characteristics that are present in macrophages after having undergone division which are not shared by a primary culture of macrophages. In fact, it the specification appears to focus on methods for maintaining macrophages in culture for extended periods of time, in a manner such that the cultured macrophages are *not* physiologically distinct from primary cultures, and thus may be used in transplantations and experiments which were previously limited due to time constraints. Therefore, the limitation 'wherein at least some of the macrophages have undergone cell division during culture *in vitro*," and the dependent limitations further defining the length of the culture period, are not considered to lend patentable weight to the product as claimed. Therefore, the product of claims 1-12 is considered to read on any composition comprising replicating macrophages.

Similarly, it is noted that claim 28 is a product-by-process claim. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself, in the instant case: a cell composition comprising replicating Kupffer cells. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Again, though the method of claim 13 requires the Kupffer cells of claim 28 to have undergone cell division *in vitro*, because such a method step does not impart a structurally or physiological distinctness to the product *as claimed*, the product of claim 28 is considered to read on any composition comprising replicating Kupffer cells.

Claims 1-8, 10-12 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Pulford et al (Clin Exp Immunol, 1980).

Pulford et al disclose the isolation and culture of Kupffer cells from the liver of adult rats and peritoneal macrophages (from the peritoneum of adult rats) (both cell types are from non-transformed, non-tumor tissue). Pulford et al report the Kupffer cells replicate and divide in culture after three days. The replicating cells stained positive for non-specific esterase and acid-phosphatase and exhibiting phagocytic properties (See Pulford et al, Pg. 69) (Claims 1-5, 8, 10-12 and 28).

Though Pulford et al do not test for or report on the expression (or lack thereof) of CD68 or TGF-beta these characteristics appear to be inherent to macrophages, including Kupffer cells and thus the peritoneal macrophages and the Kupffer cells cultured by Pulford et al inherently share the same characteristics as the composition claimed (Claims 5-7). Please note that merely because a characteristic of a cell culture is not disclosed in a reference does not make the claimed cell composition patentable. The known cell culture possesses inherent characteristics which might not be displayed in the tests used the reference. However, the cell culture disclosed appears to be the same as that claimed. Clear evidence that the cell culture of the cited prior art does not possess critical characteristics that are possessed by the claimed cell composition, would advance prosecution and might permit allowance of claims to applicants' composition comprising a particular cell type.

Claims 1-12 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Gendrault et al (Pathobiology, 1991).

Gendrault et al disclose viable cultures of human Kupffer cells derived from digested HIV-seronegative patients being treated for liver cancer (i.e. non-embryonic humans). The Kupffer cells were co-cultured with either HIV-infected CEM cells or non-infected CEM cells, in both cocultures the Kupffer cells demonstrated phagocytic properties (See Pg. 223). The Kupffer cells co-cultured with the

non-infected CEM cells are considered non-transformed. Gendrault et al report successfully maintaining the Kupffer cells in co-culture with the CEM cells for at least seventeen days (See Gendrault et al, Pg. 225, col. 1); one of ordinary skill in the art would take such to mean the Kupffer cells were inherently replicating and dividing (Claims 1-4, 8-12, 28).

Though Gendrault et al do not test for or report on the expression (or lack thereof) of CD68 or TGF-beta, or the ability to stain positive for non-specific esterase or acid-phosphatase, these characteristics appear to be inherent to Kupffer cells and thus the Kupffer cells cultured by Gendrault et al inherently share the same characteristics as the composition claimed (Claims 5-7). Please note that merely because a characteristic of a cell culture is not disclosed in a reference does not make the claimed cell composition patentable. The known cell culture possesses inherent characteristics which might not be displayed in the tests used the reference. However, the cell culture disclosed appears to be the same as that claimed. Clear evidence that the cell culture of the cited prior art does not possess critical characteristics that are possessed by the claimed cell composition, would advance prosecution and might permit allowance of claims to applicants' composition comprising a particular cell type.

Claims 1-8, 10-12 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Yoshioka et al (Veterinary Immunology and Immunopathology, 1997).

Yoshioka et al disclose a viable culture of bovine Kupffer cells obtained from digested calf livers. The cells stained positive for alpha-NBE (alpha-naphthyl butyrase esterase) (a non-specific esterase), were CD68-positive, and were phagocytic towards latex and yeast (See Yoshioka et al, Pg. 162, first full paragraph). Yoshioka et al report successfully culturing the cells and maintaining the culture for one week (See Yoshioka et al, Pg. 159, second full paragraph); one of ordinary skill in the art would take such to mean the Kupffer cells were inherently replicating and dividing (Claims 1-4, 6, 8, 10-12, 28).

Though Yoshioka et al do not test for or report on the expression (or lack thereof) of TGF-beta, or the ability to stain positive for acid-phosphatase, these characteristics appear to be inherent to Kupffer cells and thus the Kupffer cells cultured by Yoshioka et al inherently share the same characteristics as the composition claimed (Claims 5, 7). Please note that merely because a characteristic of a cell culture is not disclosed in a reference does not make the claimed cell composition patentable. The known cell culture possesses inherent characteristics which might not be displayed in the tests used the reference. However, the cell culture disclosed appears to be the same as that claimed. Clear evidence that the cell culture of the cited prior art does not possess critical characteristics that are possessed by the claimed cell composition, would advance prosecution and might permit allowance of claims to applicants' composition comprising a particular cell type.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leon B Lankford, Jr
Primary Examiner
Art Unit 1651